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| EXAMINER | |
|---|---|
| WESTERBERG, NISSA M | |
| **ART UNIT** | **PAPER NUMBER** |
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**Please find below and/or attached an Office communication concerning this application or proceeding.**

The time period for reply, if any, is set in the attached communication.

| Office Action Summary | Application No. | Applicant(s) | |
|---|---|---|---|
| | 10/525,348 | EGGERSDORFER ET AL. | |
| | Examiner | Art Unit | |
| | Nissa M. Westerberg | 1609 | |

*-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --*

**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

1)☐ Responsive to communication(s) filed on _____.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

**Disposition of Claims**

4)☒ Claim(s) 1 - 20, 26 and 27 is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) 1 - 20, 26 and 27 is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

**Application Papers**

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

**Priority under 35 U.S.C. § 119**

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

**Attachment(s)**

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

## DETAILED ACTION

### *Claim Rejections - 35 USC § 112 Second Paragraph*

1. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

2. Claims 1 – 2, 5 – 6, 20 and 26 – 27 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. The abbreviation "EGCG" is not spelled out in the claims or disclosure and is therefore vague and indefinite.

### *Claim Rejections - 35 USC § 112 First Paragraph*

3. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

4. Claims 1 – 2 and 26 – 27 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. The application does provide

adequate written description for panthethine and one metabolite of panthethine – cysteamin. However, other metabolites of panthethine are not adequately described.

5. Claims 26 and 27 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for treating type 2 diabetes in those individuals with pre-diabetes, impaired glucose tolerance or obesity, does not reasonably provide enablement for 1) the treatment of type 1 diabetes or for 2) the preventing type 2 diabetes in those individuals with pre-diabetes, impaired glucose tolerance or obesity. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to use the invention commensurate in scope with these claims.

The disclosure and claims of the application have been compared per the factors indicated in the decision *In re Wands*, 8 USPQ2nd 1400 (Fed. Cir. 1988) as to undue experimentation

The factors include:

1. The nature of the invention;
2. The breadth of the claims;
3. The predictability or unpredictability of the art;
4. The amount of direction or guidance presented;
5. The presence or absence of working examples
6. The quantity of experimentation necessary;
7. The state of the prior art; and

8. The relative skill of those skilled in the art.

Each factor is addressed below on the basis of comparison of the disclosure, the claims and the state of the art in the assessment of undue experimentation.

A. Treatment of Diabetes

1. The nature of the invention: the claims relate to a method of using a composition comprising biotin and one other component selected from pantethine or a metabolite thereof, EGCG, phytanic acid, lipoic acid and policosanol for the treatment of type 1 and 2 diabetes.

2. The breadth of the claims: the claims are broad since they recite treating patients in general suffering from type 1 or type 2 diabetes.

3. The predictability or unpredictability of the art: Type 1 diabetes is a disease that occurs when there is decreased or no production of insulin by the pancreas whereas type 2 diabetes is a condition characterized by normal or even elevated levels of insulin in the body. Due to the absence of insulin, type 1 diabetics are hyperglycemic but otherwise the metabolic activities (glycogen breakdown in the liver, gluconeogenesis in peripheral tissues and release of fatty acids from cells) of the cells are similar to those of an individual experiencing starvation. In contrast, the cells of types 2 diabetics are unable to properly respond to insulin and are insulin resistant. This leads to this condition sometimes being referred to as impaired glucose tolerance (IGT). Common

treatments for type 2 diabetes include lifestyle (diet and exercise) changes and drugs that increase insulin secretion and/or increasing the action of the insulin in peripheral tissues (Moran et al., Biochemistry, 2nd edition, 1994, p 23-25 – 23-26). Given the different etiologies of type 1 and type 2 diabetes as well as the complexity of the interactions and body systems involved, the level of predictability for a given treatment is very low.

4. Diabetes is a complicated disease to prevent and treat and has effects on many different body systems. No evidence is provided as to the efficacy of the claimed compositions in the prevention of type 2 diabetes in those individuals with pre-diabetes, impaired glucose tolerance or obesity. The mouse model used provides support for the treatment of type 2 diabetes but type 1 diabetes has a different underlying mechanism so data generated in a type 2 diabetes model does not provide support for the treatment of type 1 diabetes.

5. The presence or absence of working examples: examples of effects on genetically diabetic mice are presented that mimic type 2 diabetes with the combination of biotin and phytanic acid are presented. No working examples for treatment of type 1 diabetes are presented.

6. The quantity of experimentation necessary, the state of the prior art and the relative skill of those skilled in the art: Given the different underlying causes of type 1 and 2 diabetes, one of skill in the art would have no guidance as to how to treat type 1 diabetes. Given the complete absence of insulin production in type 1 diabetics, compounds that act to increase the activity of cells to insulin would not be expected to

have an effect. Thus, the claims as they relate to the treatment of type 1 diabetes lack enablement. The claims as they relate to type 2 diabetes are enabled.

B. Prevention of Diabetes

1. The nature of the invention: the claims relate to a method of using a composition comprising biotin and one other component selected from pantethine or a metabolite thereof, EGCG, phytanic acid, lipoic acid and policosanol for the prevention of type 2 diabetes in those individuals with pre-diabetes, IGT or obesity.

2. The breadth of the claims: the scope of the method claims includes preventing illness in patients that have pre-diabetes, IGT or are obese from developing type 2 diabetes. The verb "prevent" is defined to mean '"to stop (someone or something) from ... being in a certain state" ('prevent' from dictionary.com, accessed Aug 2, 2007), i.e. to complete eliminate a certain state.

3. The predictability or unpredictability of the art: as discussed above, type 2 diabetes arises when the cells of an individual become resistant to insulin and are in a hyperglycemic state in spite of the normal to high levels of insulin in the blood. The underlying causes of the insulin resistance are poorly understood, even by those of skill in the art. The metabolic effects of the disease occur throughout the body and the progression of the disease is poorly understood. Why lifestyle changes are sufficient for some and not for others is not known.

4. The amount of direction or guidance presented: only treatment is shown.

5. The presence or absence of working examples: no working examples for the use of the claimed compositions in the prevention of type 2 diabetes are shown.

6. The quantity of experimentation necessary, the state of the prior art and the relative skill of those skilled in the art: those of skill in the art know that obese individuals are at risk of developing type 2 diabetes. Drugs are known that can slow the progression of the disease by enabling the body to better utilize the insulin that is produced in the body. However, no drug has been shown that can bring the progression of the disease to a halt and prevent them from developing diabetes. The application does not provide any evidence as to the efficacy of the compositions in such individuals or model systems that prevents the appearance of type 2 diabetes in individuals that are obese or are suffering from pre-diabetes or IGT. Thus, the claims as they relate to the prevention of type 2 diabetes lack enablement.

***Claim Rejections - 35 USC § 102***

6. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

7. Claims 13, 16 and 17 are rejected under 35 U.S.C. 102(b) as being anticipated by Reddi et al. (*Life Sciences*, Vol 42, p 1323 – 1330, 1998). Reddi et al. uses a once daily administration of biotin at 2 mg/kg of body weight in 0.1 mL of liquid solution via a

gastric tube (p 1324, lns 1 – 3). 2 mg/kg falls within the range of 0.01 mg/kg to about 3 mg/kg recited in claim 1 and the range of about 0.35 mg to about 200 mg of biotin per mL recited in claim 17.

8. Claims 13 – 15 are rejected under 35 U.S.C. 102(b) as being anticipated by Coggeshalle et al. (*Ann N.Y. Acad Sci*, 447, p 389 – 392, 1985). Coggeshall et al. uses a solid tablet (p 392, ln 12) containing 16 mg/day of biotin (p 389, lns 16 – 17) which anticipates the claims of the instant application of a solid dosage form and one that contains about 0.35 mg to about 200 mg of biotin.

9. Claims 9 and 10 are rejected under 35 U.S.C. 102(b) as being anticipated by Fine (US Pat 6,203,819 B1, Issued Mar 20, 2001). Fine discloses a supplement comprising lipoic acid and biotin (col 10, ln 23 and ln 30) that is used in a method that assists in the metabolism of glucose for patients with diabetes and pre-diabetes.

***Claim Rejections - 35 USC § 103***

10. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

11. This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

12. The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

13. Claims 3 and 4 are rejected under 35 U.S.C. 103(a) as obvious over Gorsek (US Pat 6,103,756 A, Issued Aug 15, 2001). Gorsek discloses a supplement formulation comprising biotin and pantothenic acid (col 2, lns 44 and 45) for the treatment of diabetic retinopathy, a complication of diabetes but lacks pantethine. Pantethine is a metabolite of pantothenic acid (Hendler, S..; The Doctors' Vitamin and Mineral Encyclopedia, 1990, p 78 – 79). Therefore it would have obvious to someone of

ordinary skill in the art at the time of the instant invention to replace pantothenic acid with the metabolite pantethine in a combination of biotin with the pantethine because one would expect that they would have equivalent activity.

14. Claims 1 – 4, 26 and 27 are rejected under 35 U.S.C. 103(a) as being unpatentable over Reddi et al. and Cincotta et al. (US Pat 5,714,519, Issued Feb 3, 1998). Reddi et al. describes the use of biotin to improve glucose and insulin tolerance in genetically diabetic mice but does not describe the use of panthethine or cysteamin in the treatment of diabetes. Cincotta et al. describes the administration of panthethine (col 4, lns 27 – 34) or cysteamine (col 5, lns 16 – 17) for the treatment of hyperglycemia, glucose intolerance, insulin resistance and hyperinsulinemia but lacks biotin.

"It is prima facie obvious to combine two compositions each of which is taught by the prior art to be useful for the same purpose, in order to form a third composition to be used for the very same purpose.... [T]he idea of combining them flows logically from their having been individually taught in the prior art." In re Kerkhoven, 626 F.2d 846, 850, 205 USPQ 1069, 1072 (CCPA 1980) **MPEP 2144.06**.

Thus, it would have been obvious to someone of ordinary skill in the art at the time of the instant invention in accordance with the reasoning of the precedent to combine biotin and pantethine (or cysteamine) for the treatment of diabetes.

15. Claims 1, 2, 7, 8, 26 and 27 are rejected under 35 U.S.C. 103(a) as being unpatentable over Reddi et al. and Fluehmann et al. (European Patent Application EP

1177789 A2, published February 6, 2002). Reddi et al. describes the use of biotin to improve glucose and insulin tolerance in genetically diabetic mice but does not describe the use of phytanic acid in the treatment of diabetes. Fluehmann et al. teaches the use of phytanic acid derivatives for the treatment and prevention of diabetes or other conditions associated with impaired glucose tolerance (paragraphs 24 and 25) but lacks biotin.

"It is prima facie obvious to combine two compositions each of which is taught by the prior art to be useful for the same purpose, in order to form a third composition to be used for the very same purpose.... [T]he idea of combining them flows logically from their having been individually taught in the prior art." In re Kerkhoven, 626 F.2d 846, 850, 205 USPQ 1069, 1072 (CCPA 1980) **MPEP 2144.06**.

Thus, it would have been obvious to someone of ordinary skill in the art at the time of the instant invention in accordance with the reasoning of the precedent to combine biotin and phytanic acid for the treatment of diabetes.

16. Claims 1, 2, 9, 10, 26 and 27 rejected under 35 U.S.C. 103(a) as being unpatentable over Reddi et al., and Wessel et al. (US Pat 6,117,899, issued Sep 12, 2000). Reddi et al. describes the use of biotin to improve glucose and insulin tolerance in genetically diabetic mice but does not describe the use of lipoic acid in the treatment of diabetes. Wessel et al. teaches the use of R-(+)-α-lipoic acid (col 2, lns 35 – 37) as an antidiabetic drug but lacks biotin.

"It is prima facie obvious to combine two compositions each of which is taught by the prior art to be useful for the same purpose, in order to form a third composition to be used for the very same purpose.... [T]he idea of combining them flows logically from their having been individually taught in the prior art." In re Kerkhoven, 626 F.2d 846, 850, 205 USPQ 1069, 1072 (CCPA 1980) **MPEP 2144.06**.

Thus, it would have been obvious to someone of ordinary skill in the art at the time of the instant invention in accordance with the reasoning of the precedent to combine biotin and lipoic acid for the treatment of diabetes.

17. Claims 1, 2, 5, 6, 26 and 27 are rejected under 35 U.S.C. 103(a) as being unpatentable over Reddi et al., and Van Leare et al. (PG Pub 2003/0004215, filed June 15, 2001, published January 2, 2003). Reddi et al. describes the use of biotin to improve glucose and insulin tolerance in genetically diabetic mice but does not describe the use of epigallocatechin gallate (EGCG) in the treatment of diabetes. Van Leare et al. discloses the use of a green tea extract containing 20 wt.% catechins expressed as epigallocatechin gallate (pg 6, col 1, paragraphs 66 and 67) in a dietetic preparation for inhibiting intestinal absorption of carbohydrates but lacks biotin. Decreased absorption of carbohydrates can be beneficial to diabetics (pg 1, paragraph 3)

"It is prima facie obvious to combine two compositions each of which is taught by the prior art to be useful for the same purpose, in order to form a third composition to be used for the very same purpose.... [T]he idea of combining them flows logically from

their having been individually taught in the prior art." In re Kerkhoven, 626 F.2d 846, 850, 205 USPQ 1069, 1072 (CCPA 1980) **MPEP 2144.06**.

Thus, it would have been obvious to someone of ordinary skill in the art at the time of the instant invention in accordance with the reasoning of the precedent to combine biotin and epigallocatechin gallate for the treatment of diabetes.

18. Claims 1, 11, 12 and 26 rejected under 35 U.S.C. 103(a) as being unpatentable over Reddi et al., and Crespo et al. (*Int J Clin Pharmacol Res*, 19(4), 117 – 127, 1999). Reddi et al. describes the use of biotin to improve glucose and insulin tolerance in genetically diabetic mice but does not describe the use of policosanol in the treatment of diabetes. Crespo et al. describes the use of policosanol for the treatment of dyslipidemia associated with type 2 diabetes (p 188, col 2, lns 30 – 41) but lacks biotin. Dyslipidemia is associated with both type I and type II diabetes and results in an increase in the relative risk of coronary heart disease in comparison to the nondiabetic population (Best and O'Neal, *Drugs*, 59(5), p 1101 – 1111, 2000).

"It is prima facie obvious to combine two compositions each of which is taught by the prior art to be useful for the same purpose, in order to form a third composition to be used for the very same purpose.... [T]he idea of combining them flows logically from their having been individually taught in the prior art." In re Kerkhoven, 626 F.2d 846, 850, 205 USPQ 1069, 1072 (CCPA 1980) **MPEP 2144.06**.

Thus, it would have been obvious to someone of ordinary skill in the art at the time of the instant invention in accordance with the reasoning of the precedent to combine biotin and policosanol for the treatment of diabetes.

19. Claims 18 and 19 are rejected under 35 U.S.C. 103(a) as being unpatentable over Reddi et al. as applied to claims 1 - 12 above, and further in view of Pearson et al. (US Pat 6,261,589 B1, Issued July 17, 2001). As described above, combinations of biotin with panthethine or cysteamin, EGCG, phytanic acid, lipoic acid or policosanol are obvious combinations. None of the references describe the use of the composition in a beverage. Pearson et al. describes a composition containing a variety of nutrients in solution (as a soft drink) to support the production of and to stimulate the release of neurotransmitters and neuromodulators in the brain (col 2, lns 17 – 30) but lacks biotin in combination with panthethine or cysteamin, EGCG, phytanic acid, lipoic acid or policosanol. Thus, it would have been obvious to someone of ordinary skill in the art at the time of the instant invention to use the nutraceutical of the instant case in a beverage to achieve the physiological effect of the supplement.

20. Claims 18 and 19 are rejected under 35 U.S.C. 103(a) as being unpatentable over Reddi et al. as applied to claims 1 - 12 above, and further in view of Holbrook et al. (US Pat 6,132,795, Issued Oct 17, 2000). As described above, combinations of biotin with panthethine or cysteamin, EGCG, phytanic acid, lipoic acid or policosanol are obvious combinations. None of the references describe the use of the composition in a

food. Holbrook et al. describes the use of an isoflavone containing material and isoflavone depleted vegetable protein composition that may be used in foods as a functional ingredient (col 4, lns 21 – 22) but lacks biotin and panthethine or cysteamin, EGCG, phytanic acid, lipoic acid or policosanol. Thus, it would have been obvious to someone of ordinary skill in the art at the time of the instant invention to use the biotin comprising compositions of the instant case in a food to achieve the physiological effect of the supplement.

## ***Conclusion***

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Nissa M. Westerberg whose telephone number is (571) 270-3532. The examiner can normally be reached on M - F, 7:30 a.m. - 5 p.m. ET. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ardin H. Marschel can be reached on (571) 272-0718 or Cecilia Tsang can be reached on (571) 272-0562. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

NMW

Frederick Krass
Primary Examiner
Art Unit 1614